REMARKS

Claims 1-9 and 39-47 are pending and under examination in the above-identified application. Claim 39 has been amended to correct obvious informalities. Accordingly, the amendments do not raise an issue of new matter and entry thereof is respectfully requested. Applicant has review the rejections set forth in the Office Action mailed November 16, 2004, and respectfully traverse all grounds for the reasons that follow.

Rejections Under 35 U.S.C. § 112

Claims 1-9 and 39-47 stand rejected under 35 U.S.C. § 112, first paragraph allegedly for lacking written description. In this regard, the Office maintains that the application fails to describe any identifying characteristics regarding the receptors, ligands or the receptor variant except for the generic definitions. *University of California v. Eli Lilly and Co.* is relied on as support for this rejection.

Applicant respectfully directs the Examiner's attention to the more recent Federal Circuit decisions that have further clarified the *Lilly* decision. In the recent decision of *Moba v. Diamond Automation*, 325 F.3d 1306, 66 USPQ2d 1429 (Fed.Cir. 2003) the Federal Circuit stated:

> [C]ase law reflects two applications of [the written description requirement,] . . . "[t]he function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him. . . . In that setting, the written description is the metric against which a subsequently added claim is measured to determine if it is due the priority date of the original patent. . . . The second application of the written description requirement is reflected in Regents of the *University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997). There, this court invoked the written description requirement in a case without priority issues, [requiring a] precise definition of a DNA sequence in the patent specification. In more recent cases, however, this court has distinguished *Lilly*. . . . The *Lilly* disclosure rule does not require a particular form of disclosure because one of skill could determine from the specification that the inventor possessed the invention at the time of filing.

Id. at 1319.

Similarly, in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002), after initially holding that a reference to specified biological material in a public depository was not a sufficient written description, the court on rehearing indicated that *Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement and held the written description requirement may be satisfied if, in the knowledge of the art, the disclosed function is sufficiently correlated to a particular, known structure.

In its first pronouncement following *Enzo*, the Federal Circuit again followed this rationale in *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1399 (Fed. Cir. 2003). The Federal Circuit recently extended this rationale to binding polypeptides such as antibodies in *Noelle v. Lederman*, Case No. 02-1187 (Fed. Cir., Jan. 20, 2004). The Court in *Noelle* stated that written description for antibodies relying on functional characteristics can be met if function is coupled with a disclosed correlation to a known structure. This extension between a structure and functional relationship also was embraced in *University of Rochester v. G.D. Searle & Co.*, where the Federal Circuit, while affirming the broad principles of *Lilly* as it had done in *Enzo Biochem II*, acknowledged that molecular biology is different than chemistry and may not require the same degree of structure in a distinguishing description:

> [W]here there might be some basis for finding a written-description requirement to be satisfied in a genetics case based on the complementariness of a nucleic acid and, for example, a protein, that correspondence might be less clear in a non-genetic situation . . . . DNA and RNA are each made up of just four building blocks that interact with each other in a highly predictable manner . . . . Given the sequence of a single strand of DNA or RNA, it may therefore have become a routine matter to envision the precise sequence of a 'complementary' strand that will bind to it. Therefore, disclosure of a DNA sequence might support a claim to the complementary molecules that can hybridize to it. The same is not necessarily true in the chemical arts more generally.

358 F.3d 916, 925 (Fed. Cir. 2004). While not eliminating the demands of the written description requirement, the *Rochester* court indicated that applicants have some flexibility in the "mode selected for compliance." *Id.* at 928.

Claim 1 is directed to method for determining binding of a receptor to one or more ligands. The method includes contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population. Applicants have complied with the written description requirement for this molecular biology invention by a mode adequate to show that Applicant was in possession of the invention at the time the application was filed.

Unlike *Lilly*, Applicant has not claimed a receptor, ligand or receptor variant population. Rather, Applicant has claimed a method and it the method has been adequately described. The molecules employed in the method are sufficiently described in the application because that is as sufficient as the technology requires. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991). Applicant's remarks and evidence of record demonstrate that an adequate description of the method of the invention does not require a detailed description of the ligand, receptor or receptor variant because any of the molecules or classes of molecules described in the application are sufficient with only a general knowledge of its structure. Accordingly, the application adequately describes the claimed invention and withdrawal of this ground of rejection is respectfully requested.

Claims 5 and 43 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly introducing new matter. The Office asserts that the term "optimal binding activity to said one or more ligands relative to a parent receptor variant population" lacks support in the specification and claims as originally filed.

Applicants submit that the objected term is adequately supported in the application as filed. For example, the objected term can be found in the application at, for example, page 10, line 23 through page 11, line 14, and particularly at page 10, lines 31-32, as well as other descriptions throughout the application. Accordingly, claims 5 and 43 are supported in the application as filed and withdrawal of this ground of rejection is respectfully requested.

Claims 1 and 39 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. In this regard, the Office asserts that the claim method of determining is either missing a method step or is intended to identify the entire population of receptors.

Applicants submit that the claim is clear as written. Claim 1 is directed to method for determining binding of a receptor to one or more ligands. The method includes contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population. The application describes that binding to a collective population can be to some or all members of the population. Therefore, these claims are clear as written and withdrawal of this ground of rejection is respectfully requested. Further, the rejection of claim 39 for allegedly lacking antecedent basis has been rendered moot by the amendment above.

Claims 2 and 40 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The Office asserts that the claims are unclear as to whether the collective receptor variant population is the population bound to the one or more ligands or the original collective receptor variant population irrespective of its binding to the ligand.

Applicants submit that the claim is clear as written. Claim 2 is directed to a method for determining binding of a receptor to one or more ligands that includes contacting a collective receptor variant population with the one or more ligands; detecting binding of the one or more ligands to said collective receptor variant population and further includes dividing the collective receptor variant population into two or more subpopulations, contacting one or more of said two or more subpopulations with said one or more ligands and detecting one or more receptor variant subpopulations having binding activity to said one or more ligands. Therefore, these claims are clear as written and withdrawal of this ground of rejection is respectfully requested.

Claims 5 and 43 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. In this regard, the Office alleges that the term "optimal binding activity" is a relative term and that the specification has not disclosed optimal binding relative to a parent receptor of the receptor variant population.

Applicants submit that the claim is clear as written. Further, and as pointed out previously, the term "optimal binding" is described throughout the specification. Moreover, the term is explicitly defined at, for example, page 10, line 23 through page 11, line 14. In light of these clear teachings as well as the plain meaning of the claim language, Applicants contend that

the claim is sufficiently clear and distinctly claims the subject matter which Applicants' regard as the invention. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 1-8 and 39-46 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lerner et al., U.S. Patent No. 5, 426,856. Claims 1-5, 8-9, 39-43 and 46-47 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Houghten et al., U.S. Patent No. 6,287,787. Further, claims 1, 6-7, 9, 39, 44-45 and 47 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Bergsma et al., U.S. Patent No. 5,912,335. The Office alleges that these references describe all elements of the claimed invention.

When lack of novelty is based on a printed publication that is asserted to describe the same invention, a finding of anticipation requires that the publication describe all of the elements of the claims. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1349, 48 U.S.P.Q.2d 1225, (Fed. Cir. 1998) (quoting *Shearing v. Iolab Corp.*, 975 F.2d 1541, 1544-45, 24 U.S.P.Q.2d 1133, 1136 (Fed. Cir. 1992)). To establish a prima facie case of anticipation, the Examiner must show that the single reference cited as anticipatory art describes all the elements of the claimed invention.

Claim 1 is directed to method for determining binding of a receptor to one or more ligands. The method includes contacting a collective receptor variant population with said one or more ligands and detecting binding of said one or more ligands to said collective receptor variant population.

The Office fails to particularly point out each of the elements claimed by in the invention that are allegedly described in Lerner et al., Houghten et al. or Bergsma et al. In particular, none of the cited references describes contacting a collective receptor variant population with one or more ligands. Because none of the cite references describe all elements of the claimed invention, neither Lerner et al., Houghten et al. or Bergsma et al. can anticipate the invention as claimed. Therefore, Applicants respectfully request that this ground of rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-9 and 39-47 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Bergsma et al, U.S. Patent No. 5,912,335 and Hudson et al., U.S. Patent No. 5,844,094. Bergsma et al. is applied as above under the § 102 rejection. Hudson et al. is alleged to describe method of producing novel polypeptides with modified binding activity, including dividing the population into subpopulations. The Office alleges that it would have been obvious to combine Bergsma et al. with Hudson et al. to arrive at a method that uses repeated detection and screening steps because increased affinity would have been obtained.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 180 USPQ 580 (C.C.P.A. 1974); M.P.E.P. §2143.03.

Applicants respectfully submit that the Office has not established a *prima facie* case of obviousness, at least because all the elements of the claimed method for determining binding of a receptor to one or more ligands are not taught or suggested by the cited art. The pending claims recite contacting a collective receptor variant population with the one or more ligands and detecting binding of the one or more ligands to said collective receptor variant population. As described previously, the primary reference to Bergsma et al. However, the cited references, alone or in combination, fail to teach or suggest contacting a collective receptor variant population with one or more ligands. In the absence of a teaching or suggestion in the cited references of each element of the claimed ligation probes, the Office has not established a *prima facie* case of obviousness of any of the claims under 35 U.S.C. § 103(a). Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

CONCLUSION

In light of the Amendments and Remarks herein, Applicant submits that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper,

including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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